**FIG. 2**

1	1	T	P	V	S	E	K	O	L	A	E	V	V	A	N	T	I	T	P	L	M	K	A	Q	S	V	P	G	M	A	V	A	V	I	Y	Q	G	K	P	H	Y	T	F	G	K	A	D	I	A	N
2	1	A	K	T	E	Q	O	I	A	D	I	V	N	R	T	I	T	P	L	M	K	A	Q	S	V	P	G	M	A	V	A	V	I	Y	E	G	K	P	H	Y	T	F	G	K	A	D	I	A		
3	1	T	K	T	E	L	Q	V	A	T	A	V	D	G	I	I	Q	P	M	L	K	E	Y	R	I	P	G	M	A	V	A	V	I	Y	D	G	K	P	H	Y	T	F	G	K	A	D	I	A		
4	1	Y	A	R	G	E	A	P	L	T	A	A	V	D	G	I	I	Q	P	M	L	K	E	Y	R	I	P	G	M	A	V	A	V	I	Y	D	G	K	P	H	Y	T	F	G	K	A	D	I	A	
1	51	N	K	P	V	T	Q	T	L	F	E	L	G	S	I	S	K	T	F	T	G	V	L	G	G	D	A	I	A	R	G	E	I	S	L	D	D	A	V	T	R	Y	W	P	E	L	T	G	K	
2	51	N	H	P	V	T	Q	T	L	F	E	L	G	S	I	S	K	T	F	T	G	V	L	G	G	D	A	I	A	R	G	E	I	S	L	D	D	A	V	T	R	Y	W	P	E	L	T	G	K	
3	51	G	R	P	V	T	E	N	T	L	F	E	L	G	S	I	S	K	T	F	T	G	V	L	G	G	D	A	I	A	R	G	E	I	S	L	D	D	A	V	T	R	Y	W	P	E	L	T	G	K
4	51	G	Q	R	V	S	E	Q	T	L	F	E	L	G	S	I	S	K	T	F	T	G	V	L	G	G	D	A	I	A	R	G	E	I	S	L	D	D	A	V	T	R	Y	W	P	E	L	T	G	K
1	101	W	Q	G	I	R	M	L	D	L	A	T	T	Y	T	A	G	G	L	P	L	Q	V	P	D	E	V	T	D	N	A	S	L	L	R	F	Y	Q	N	W	Q	P	Q	W	K	P	G	T	R	
2	101	W	R	G	I	S	L	H	L	A	T	T	Y	T	A	G	G	L	P	L	Q	V	P	D	E	V	T	D	N	A	S	L	L	R	F	Y	Q	N	W	Q	P	Q	W	K	P	G	T	R		
3	101	W	K	D	V	K	M	L	H	L	A	T	T	Y	T	A	G	G	L	P	L	Q	V	P	D	E	V	T	D	N	A	S	L	L	R	F	Y	Q	N	W	Q	P	Q	W	K	P	G	T	R	
4	101	F	D	G	V	T	M	A	E	L	A	T	T	Y	T	A	G	G	L	P	L	Q	V	P	D	E	V	T	D	N	A	S	L	L	R	F	Y	Q	N	W	Q	P	Q	W	K	P	G	T	R	
1	151	A	N	A	S	I	G	L	F	G	A	L	A	V	K	P	S	G	M	P	Y	E	Q	A	M	T	T	R	V	L	K	P	L	K	L	D	H	T	W	I	N	V	P	K	A	E	E	A	H	
2	151	A	N	S	S	I	G	L	F	G	A	L	A	V	K	P	S	G	M	P	Y	E	Q	A	M	T	T	R	V	L	K	P	L	K	L	D	H	T	W	I	N	V	P	K	A	E	E	A	H	
3	151	S	N	A	S	I	G	L	F	G	A	L	A	V	K	P	S	G	M	P	Y	E	Q	A	M	T	T	R	V	L	K	P	L	K	L	D	H	T	W	I	N	V	P	K	A	E	E	A	H	
4	151	S	N	P	S	I	G	L	F	G	A	L	A	V	K	P	S	G	M	P	Y	E	Q	A	M	T	T	R	V	L	K	P	L	K	L	D	H	T	W	I	N	V	P	K	A	E	E	A	H	
1	201	W	G	Y	R	D	G	K	A	V	R	V	S	P	G	M	L	D	A	E	A	Y	G	V	K	T	N	V	Q	D	M	A	N	W	V	M	A	N	M	D	P	E	S	L	G	D	A	L		
2	201	W	G	Y	L	E	G	K	P	V	H	V	S	P	G	M	L	D	A	E	A	Y	G	V	K	T	N	V	Q	D	M	A	N	W	V	M	A	N	M	D	P	E	S	L	G	D	A	L		
3	201	W	G	Y	K	D	G	K	P	V	R	V	T	L	G	M	L	G	E	E	A	Y	G	V	K	T	N	V	Q	D	M	A	N	W	V	M	A	N	M	D	P	E	S	L	G	D	A	L		
4	201	Y	G	Y	K	E	D	K	P	V	R	V	T	L	G	M	L	G	E	E	A	Y	G	V	K	T	N	V	Q	D	M	A	N	W	V	M	A	N	M	D	P	E	S	L	G	D	A	L		
1	251	G	I	A	L	A	Q	S	R	Y	W	R	I	G	S	M	Y	Q	G	L	G	W	E	M	L	N	W	P	V	E	A	N	T	V	E	G	S	D	S	K	V	A	L	A	P	L				
2	251	G	I	E	L	A	Q	S	R	Y	W	R	I	G	S	M	Y	Q	G	L	G	W	E	M	L	N	W	P	V	E	A	N	T	V	E	G	S	D	S	K	V	A	L	A	P	L				
3	251	A	I	I	A	S	Q	S	R	Y	W	R	I	G	S	M	Y	Q	G	L	G	W	E	M	L	N	W	P	V	E	A	N	T	V	E	G	S	D	S	K	V	A	L	A	P	L				
4	249	R	I	A	L	T	H	T	G	F	Y	S	V	G	D	M	T	Q	G	L	G	W	E	S	Y	A	Y	P	L	T	E	Q	A	L	L	A	G	N	S	P	A	V	S	F	Q	A	N			
1	301	V	N	P	A	P	P	A	V	K	A	S	W	V	H	K	T	G	S	T	G	G	F	G	S	Y	V	A	F	I	P	E	K	Q	I	G	I	V	M	L	A	N	K	S	Y					
2	301	L	V	P	A	P	A	V	K	A	S	W	V	H	K	T	G	S	T	G	G	F	G	S	Y	V	A	F	I	P	E	K	Q	I	G	I	V	M	L	A	N	K	S	Y						
3	301	L	V	P	A	P	A	V	K	A	S	W	V	H	K	T	G	S	T	G	G	F	G	S	Y	V	A	F	I	P	E	K	Q	I	G	I	V	M	L	A	N	K	S	Y						
4	299	F	A	V	P	K	A	M	G	E	Q	R	L	Y	N	K	T	G	S	T	G	G	F	G	A	Y	V	A	F	I	P	E	K	Q	I	G	I	V	M	L	A	N	K	S	Y					
1	351	E	A	A	Y	H	I	L	E	A	L	Q																																						
2	351	K	A	A	Y	D	I	L	Q	A	L	R																																						
3	351	Q	A	A	Y	D	I	L	Q	A	L	R																																						
4	349	K	A	A	Y	D	I	L	Q	A	L	R																																						

1	Enterbacter cloacae	P05364	(X03866)	(SEQ ID NO:1)
2	Citrobacter freundii	P05193	(X07274)	(SEQ ID NO:2)
3	Yersinia enterocolitica	P45460	(X63149)	(SEQ ID NO:3)
4	Klebsiella pneumoniae	Q48437	(X77455)	(SEQ ID NO:4)

FIG. 3

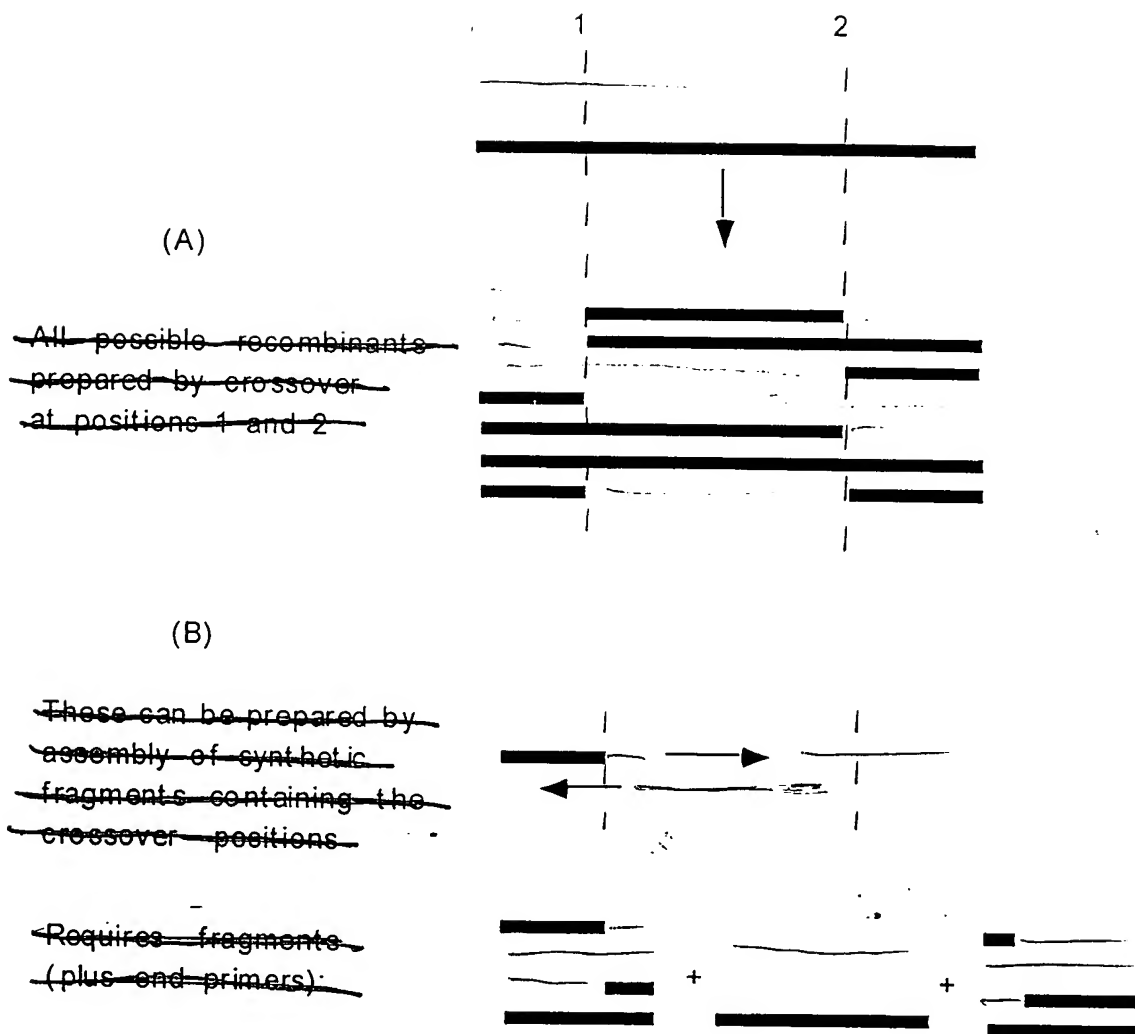
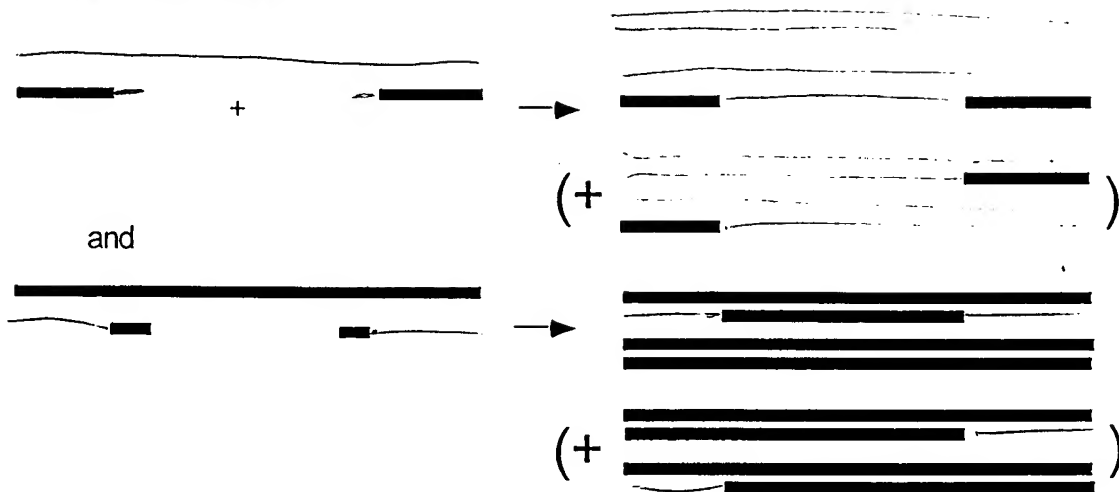


FIG. 7

(A) ~~Extension of synthetic fragments against a parent template strand and gap repair.~~

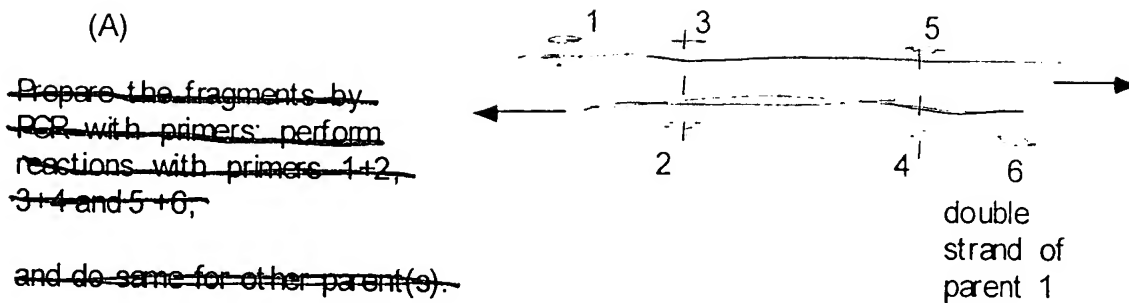


~~heteroduplex recombination~~
~~(remove parent homoduplexes)~~

(B)

library of recombinants
with crossovers in regions
of non-identity

FIG. 8



(B)

Reassemble fragments in a pool, by PCR with 1+ 6

FIG. 9

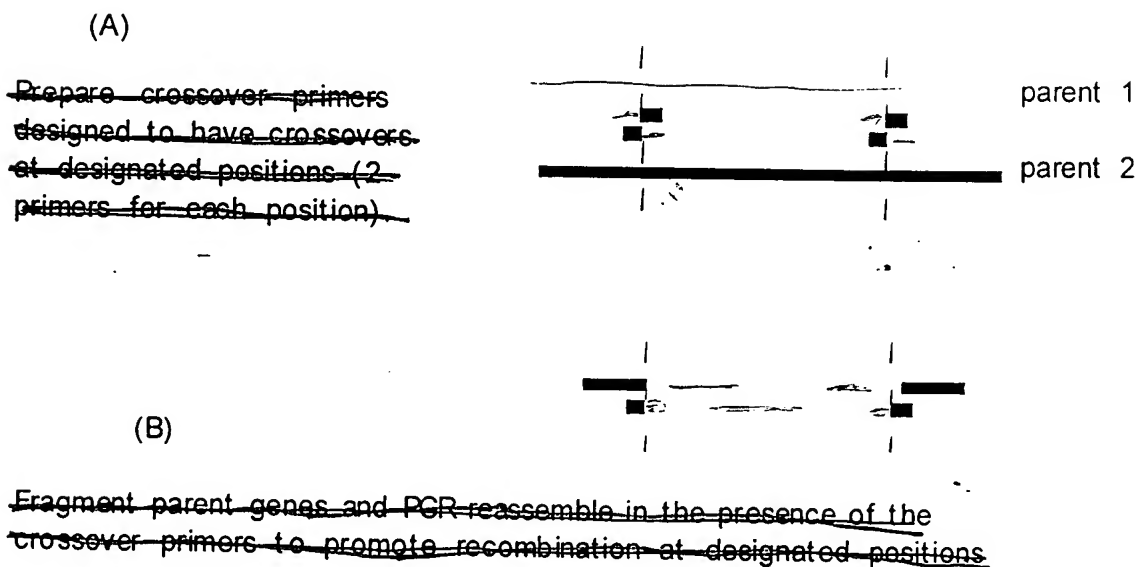
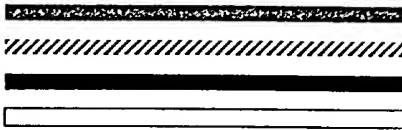


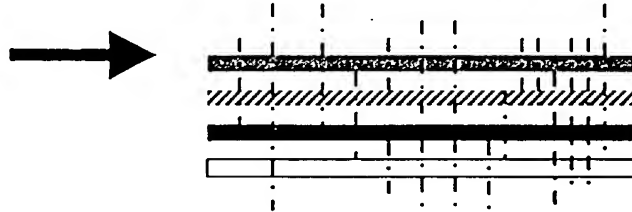
FIG. 10

Recombinant search algorithm

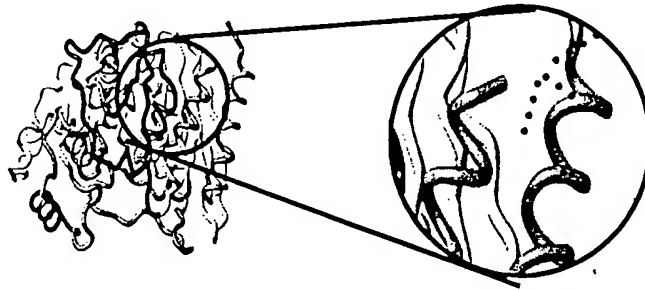
1. ~~Align parent sequences
with template structure~~



2. ~~Determine all possible crossover points
according to sequence identity algorithm~~



3. ~~Calculate coupling matrix~~



4. ~~Pick start parent at random
and copy to offspring until a
possible cut point is reached~~

5. ~~Pick random number, if less than p ,
copy random new parent until next cut
point is reached.~~

6. ~~Determine crossover
disruption of offspring gene.~~

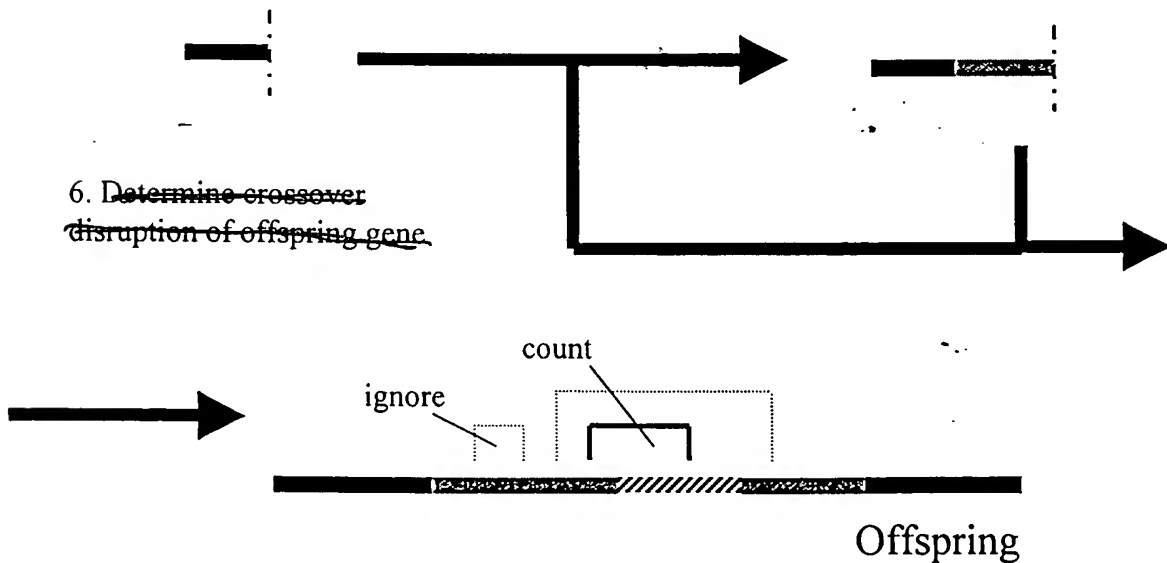


FIG. 12

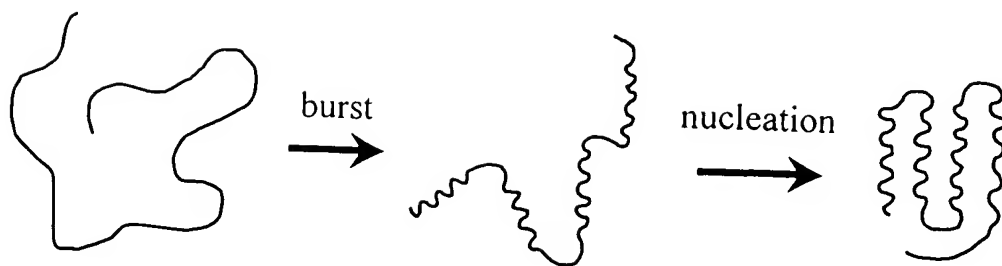


FIG. 18

~~The contact map shows residues that are distant (black) and residues that are close (white). If a given segment, folds an above average number of residues into a given sphere size, then it is compact.~~

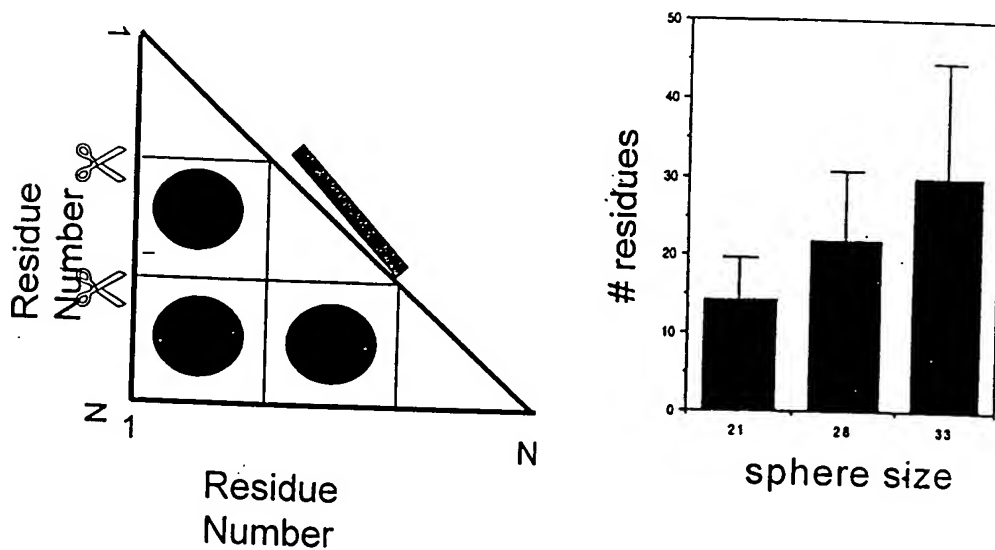


FIG. 19

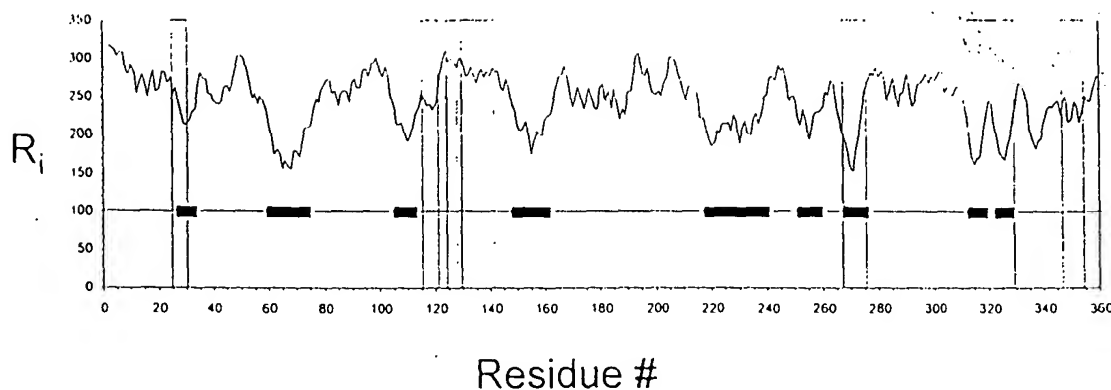
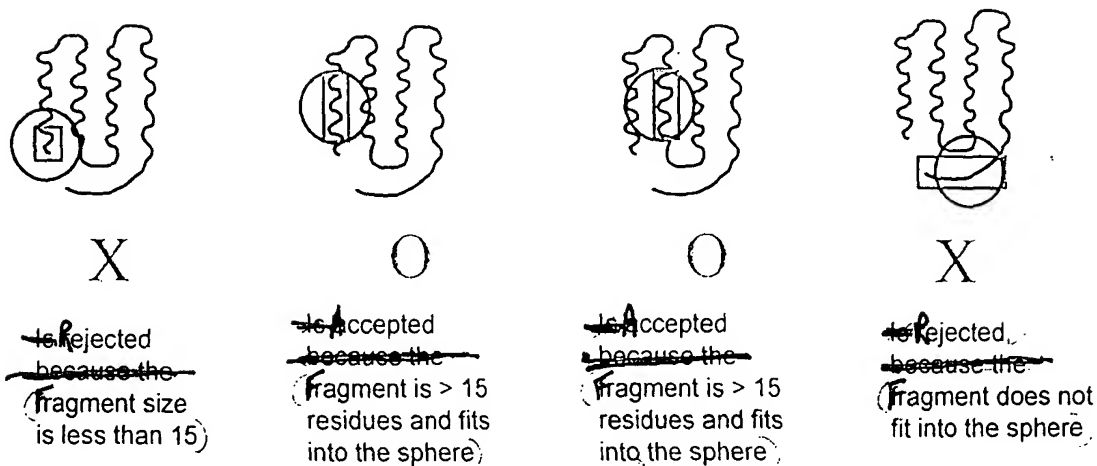


FIG. 22



~~(1) Pick a sphere size (21 angstroms, like Go-Oilbert) and a disruption threshold; (2) Scan protein using segments at least the average number of residues for that sphere size or greater (e.g., >15 for 21 angstrom sphere); (3) Check the disruption of all the compact fragments identified in step 2. If the fragment has a disruption above a threshold value, keep it; otherwise, throw it out; (4) If the compact unit is disruptive, increment the schema disruption measure for all of the residues in the fragment by one. This indicates that crossovers within the fragment are disfavored.~~

FIG. 23

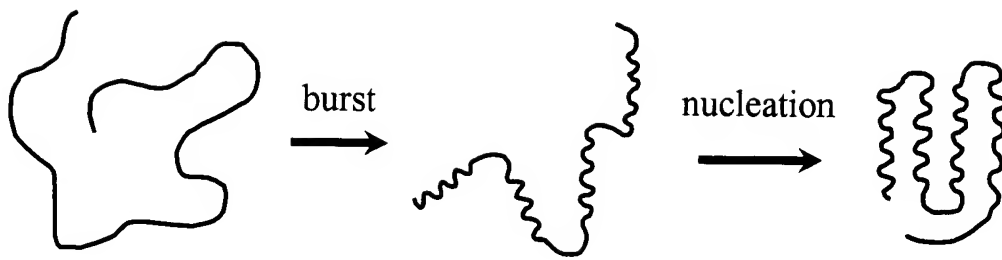


FIG. 18

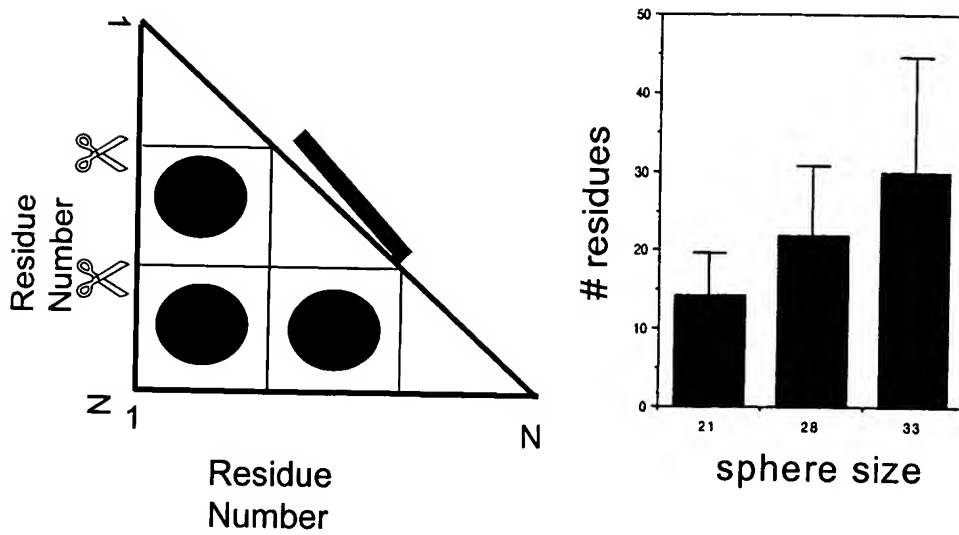


FIG. 19

Recombinant search algorithm

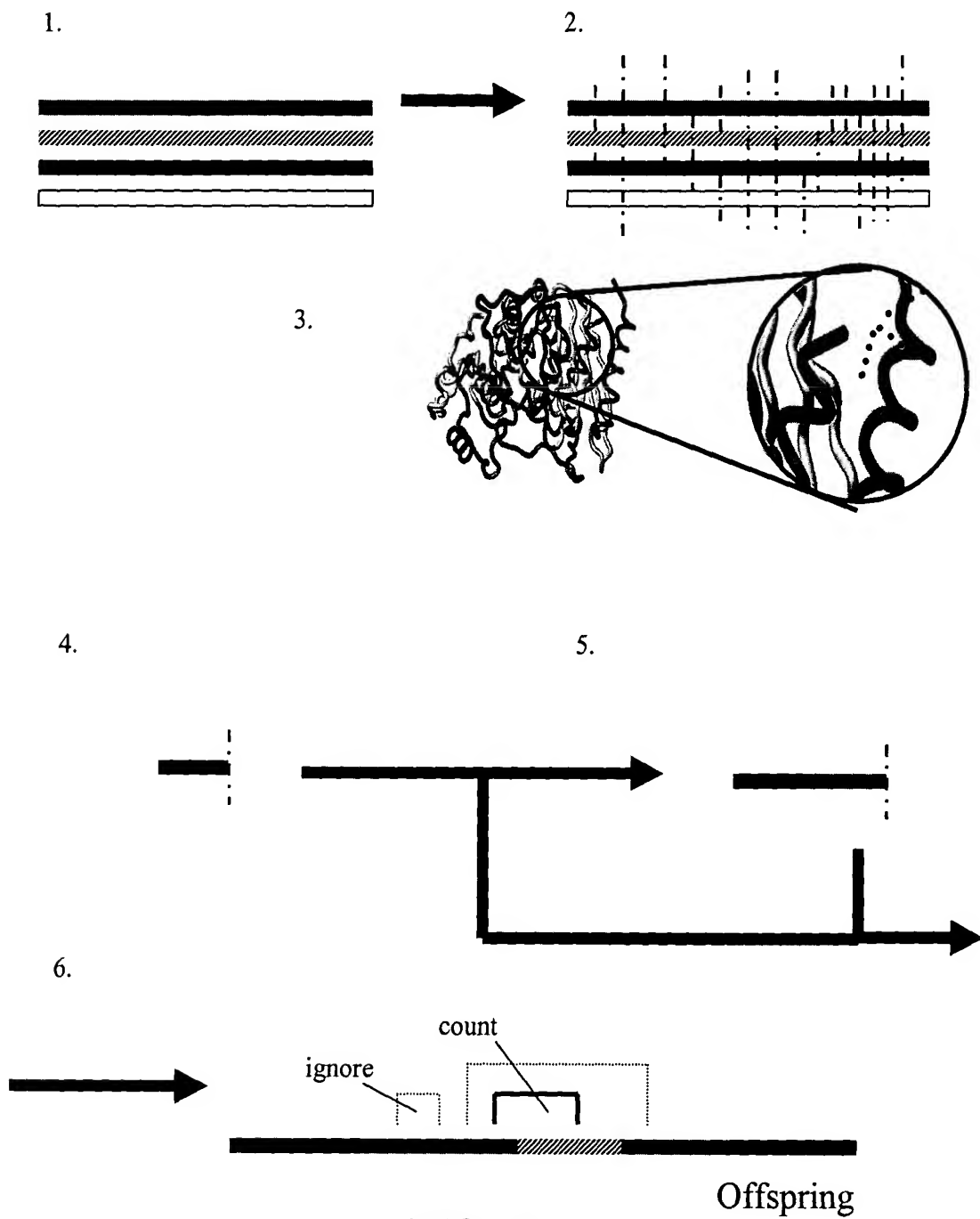
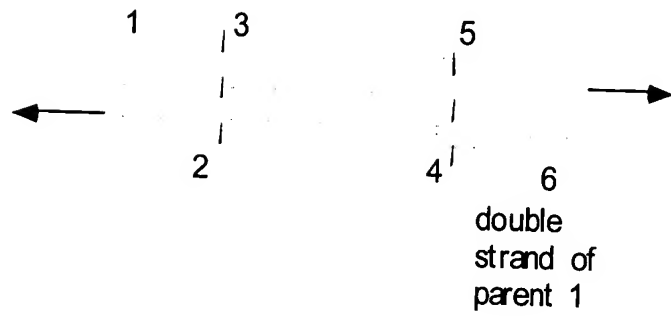


FIG. 12

(A)



(B)

Reassemble fragments in a pool, by PCR with 1+ 6

FIG. 9

(A)



(B)



FIG. 10

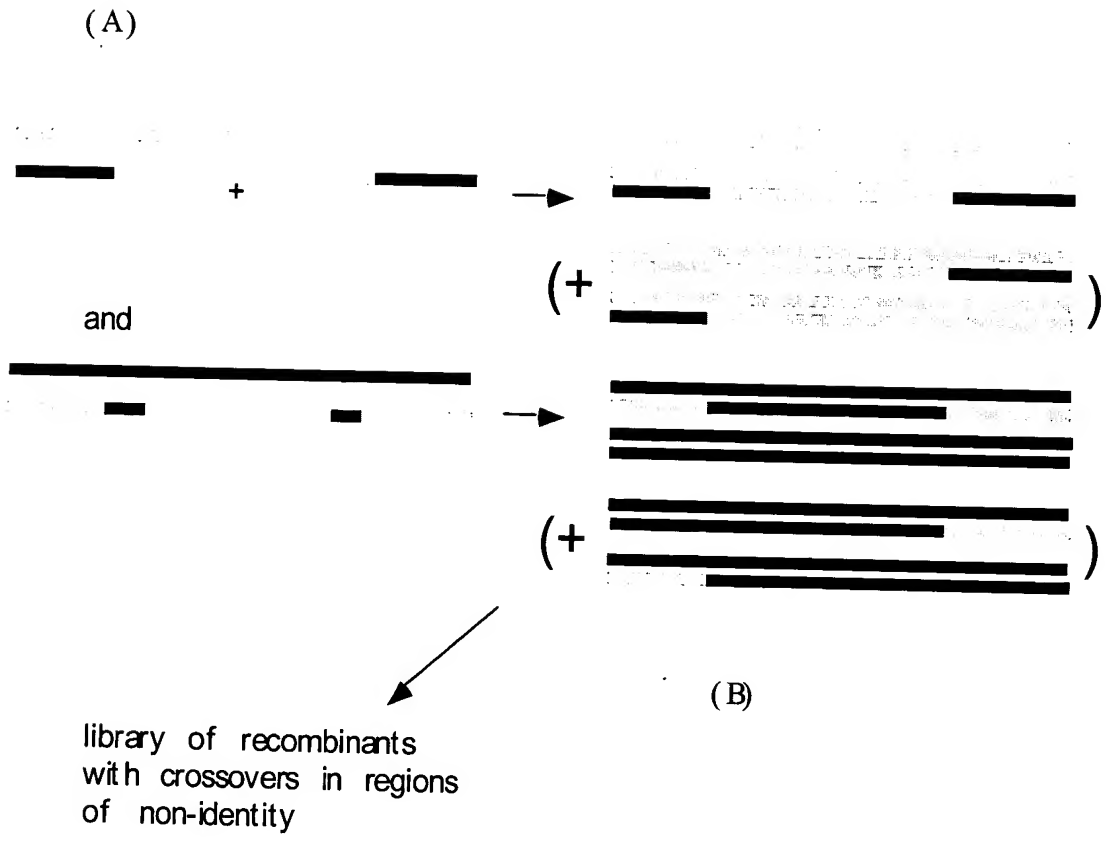


FIG. 8

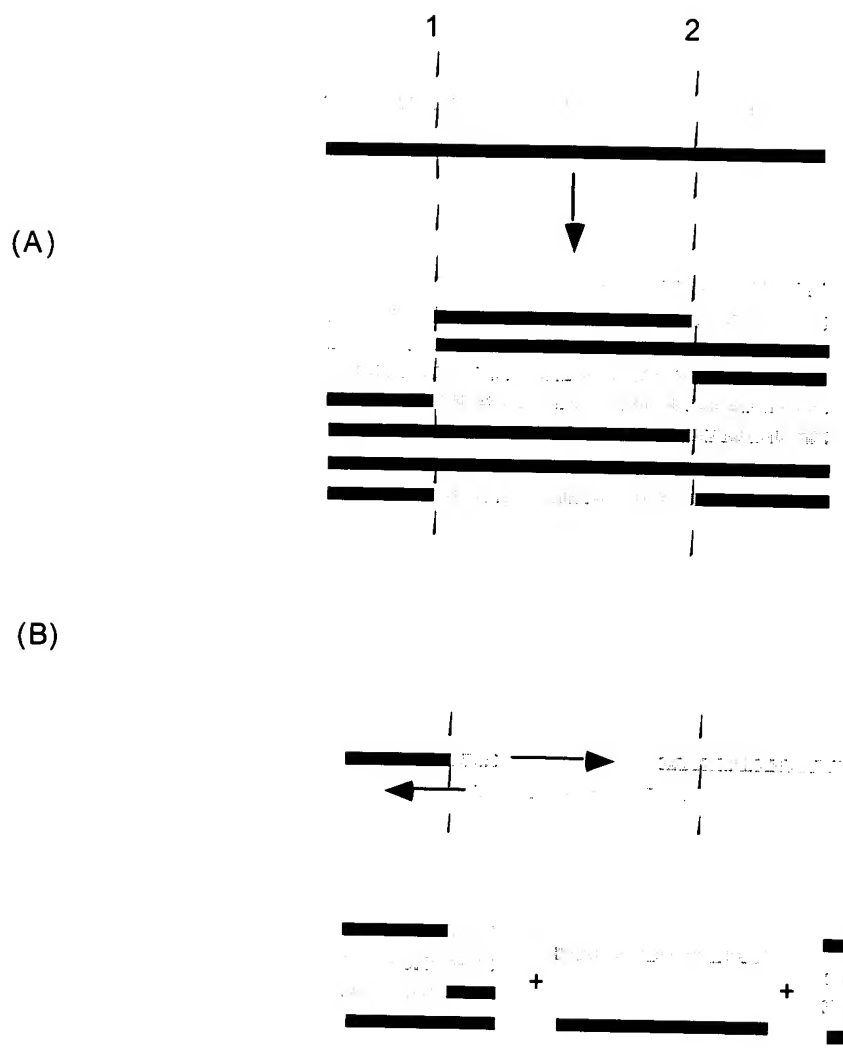
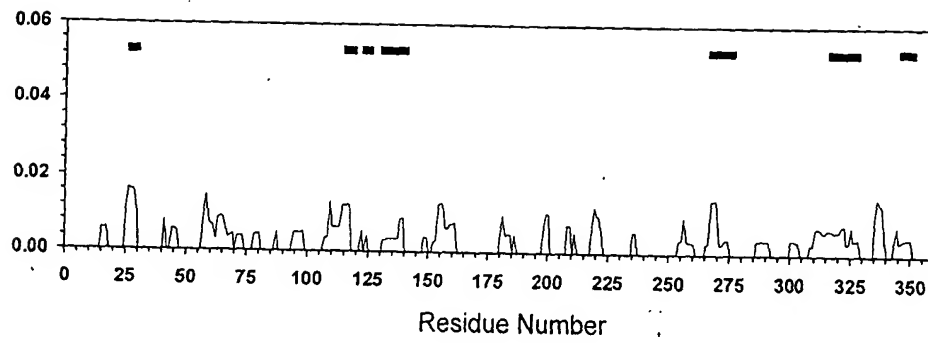
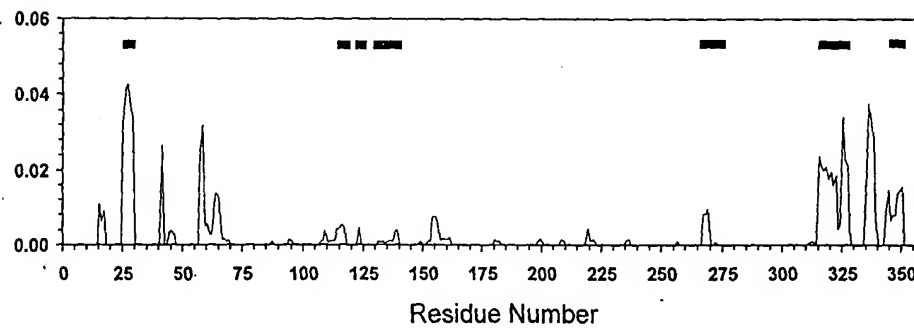


FIG. 7

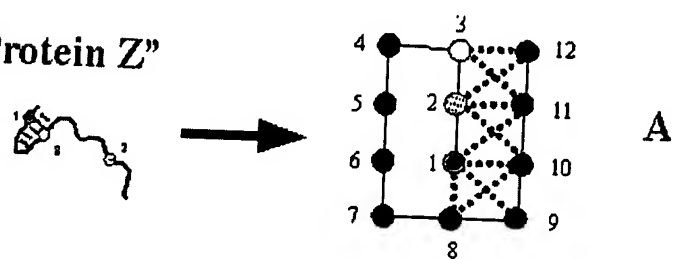
**FIG. 4C****FIG. 4D**

1	1	T	P	V	S	E	K	Q	L	A	E	V	V	A	N	T	I	T	P	L	M	K	A	O	S	V	P	G	M	A	V	A	V	I	Y	O	G	K	P	H	Y	Y	T	F	G	K	A	D	I	A	A	
2	1	A	K	L	T	E	L	Q	V	A	I	V	N	N	T	I	T	P	L	L	E	K	Q	A	I	P	G	M	A	V	A	V	I	Y	E	G	K	P	Y	F	T	W	G	M	A	D	I	K	A			
3	1	Y	A	R	G	E	A	P	L	T	A	A	V	D	G	I	Q	P	M	L	K	E	Y	R	I	P	G	M	A	V	A	V	I	L	K	D	G	K	A	H	Y	F	N	Y	G	M	A	D	I	R		
4	51	N	K	P	V	T	P	Q	T	L	F	E	L	G	S	I	S	K	T	F	T	G	V	L	G	G	D	A	I	A	R	G	E	I	S	L	D	D	A	V	T	R	Y	W	P	O	L	T	G	K		
1	51	G	R	P	V	T	E	N	T	L	F	E	L	G	S	V	S	K	T	F	T	G	V	A	L	G	G	D	R	I	A	M	O	T	G	I	M	N	L	N	D	P	V	T	E	Y	A	P	E	L	T	G
2	51	G	R	P	V	T	E	N	T	L	F	E	L	G	S	V	S	K	T	F	T	G	V	A	L	G	G	D	R	I	A	M	O	T	G	I	M	N	L	N	D	P	V	T	E	Y	A	P	E	L	T	G
3	51	G	R	P	V	T	E	N	T	L	F	E	L	G	S	V	S	K	T	F	T	G	V	A	L	G	G	D	R	I	A	M	O	T	G	I	M	N	L	N	D	P	V	T	E	Y	A	P	E	L	T	G
4	101	W	Q	G	I	S	L	H	L	A	T	T	Y	T	A	G	G	L	P	L	Q	I	P	D	E	V	T	D	N	A	S	L	L	R	E	Y	Q	N	W	Q	P	Q	W	K	P	G	A	K	R			
1	101	W	K	D	V	K	M	L	H	L	A	T	T	Y	T	A	G	G	L	P	L	Q	I	P	D	E	V	T	D	N	A	S	L	L	R	E	Y	Q	N	W	Q	P	Q	W	K	P	G	A	K			
2	101	F	D	G	V	T	M	A	E	L	A	T	T	Y	T	A	G	G	L	P	L	Q	I	P	D	E	V	T	D	N	A	S	L	L	R	E	Y	Q	N	W	Q	P	Q	W	K	P	G	A	K			
3	101	F	D	G	V	T	M	A	E	L	A	T	T	Y	T	A	G	G	L	P	L	Q	I	P	D	E	V	T	D	N	A	S	L	L	R	E	Y	Q	N	W	Q	P	Q	W	K	P	G	A	K			
4	151	A	N	S	I	G	L	F	G	A	L	A	V	K	P	S	G	M	S	Y	E	E	A	M	T	R	V	L	K	P	L	K	L	D	H	T	W	I	N	V	P	K	A	E	E	A	H	Y				
1	151	A	N	S	I	G	L	F	G	A	L	A	V	K	P	S	G	M	S	Y	E	E	A	M	T	R	V	L	K	P	L	K	L	D	H	T	W	I	N	V	P	K	A	E	E	A	H					
2	151	S	N	P	S	I	G	L	F	G	A	L	A	V	K	P	S	G	M	S	Y	E	E	A	M	T	R	V	L	K	P	L	K	L	D	H	T	W	I	N	V	P	K	A	E	E	A					
3	151	S	N	P	S	I	G	L	F	G	A	L	A	V	K	P	S	G	M	S	Y	E	E	A	M	T	R	V	L	K	P	L	K	L	D	H	T	W	I	N	V	P	K	A	E	E						
4	151	S	N	P	S	I	G	L	F	G	A	L	A	V	K	P	S	G	M	S	Y	E	E	A	M	T	R	V	L	K	P	L	K	L	D	H	T	W	I	N	V	P	K	A	E							
1	201	W	G	Y	L	E	G	K	P	V	R	V	T	P	G	V	L	A	A	E	A	Y	G	I	K	T	G	S	A	D	L	L	K	F	T	E	A	N	M	G	Y	Q	.	.	G	D	A	L				
2	201	W	G	Y	L	E	G	K	P	V	R	V	T	P	G	V	L	A	A	E	A	Y	G	I	K	T	G	S	A	D	L	L	K	F	T	E	A	N	M	G	Y	Q	.	.	G	D	A					
3	201	W	G	Y	L	E	G	K	P	V	R	V	T	P	G	V	L	A	A	E	A	Y	G	I	K	T	G	S	A	D	L	L	K	F	T	E	A	N	M	G	Y	Q	.	.	G	D						
4	201	Y	G	Y	K	E	D	K	P	V	R	V	T	P	G	V	L	A	A	E	A	Y	G	I	K	T	G	S	A	D	L	L	K	F	T	E	A	N	M	G	Y	Q	.	.	G	D						
1	251	G	I	L	A	Q	S	R	Y	W	R	I	G	S	M	Y	Q	G	L	G	W	E	M	L	N	W	P	V	E	A	N	T	V	E	G	S	D	S	K	V	A	L	A	P	L							
2	251	G	I	L	A	Q	S	R	Y	W	R	I	G	S	M	Y	Q	G	L	G	W	E	M	L	N	W	P	V	E	A	N	T	V	E	G	S	D	S	K	V	A	L	A	P								
3	251	A	I	L	A	S	O	S	R	Y	F	O	A	G	D	M	F	O	G	L	G	W	E	M	Y	S	W	P	I	N	P	O	Q	G	V	I	A	D	S	G	N	P	A	V								
4	249	R	I	L	A	L	T	H	T	G	F	Y	S	V	G	D	M	T	Q	G	L	G	W	E	S	Y	A	P	L	T	E	Q	A	L	L	A	G	N	S	P	A	V										
1	301	V	N	P	A	P	A	V	K	A	S	W	V	H	K	T	G	S	T	G	G	F	G	S	Y	V	A	F	I	P	E	K	Q	I	G	I	V	M	L	A	N	T	S	Y								
2	301	V	N	P	A	P	A	V	K	A	S	W	V	H	K	T	G	S	T	G	G	F	G	S	Y	V	A	F	I	P	E	K	Q	I	G	I	V	M	L	A	N	T	S									
3	301	L	V	P	A	Q	P	A	V	R	A	S	W	V	H	K	T	G	A	T	N	G	F	G	A	Y	I	V	F	I	P	E	E	K	I	A	I	V	M	L	A	N	T									
4	289	F	A	V	P	K	A	M	G	E	Q	R	L	Y	N	K	T	G	S	T	G	F	G	A	Y	V	A	F	V	P	A	R	G	I	A	I	V	M	L	A	N	T										
1	351	E	A	A	Y	H	I	L	E	A	L	Q																																								
2	351	K	A	A	Y	H	I	L	E	A	L	Q																																								
3	351	Q	A	A	Y	H	I	L	E	A	L	Q																																								
4	349	K	A	A	Y	H	I	L	E	A	L	Q																																								

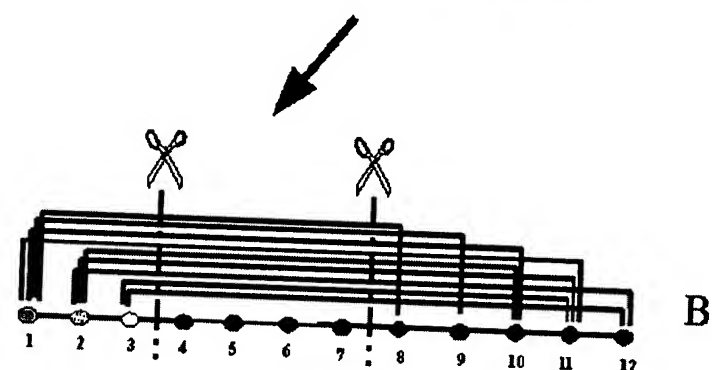
1	Enterobacter cloacae	P05364	(SEQ ID NO: 1)
2	Citrobacter freundii	P05193	(SEQ ID NO: 2)
3	Yersinia enterocolitica	P45460	(SEQ ID NO: 3)
4	Klebsiella pneumoniae	Q48437	(SEQ ID NO: 4)

FIG. 3

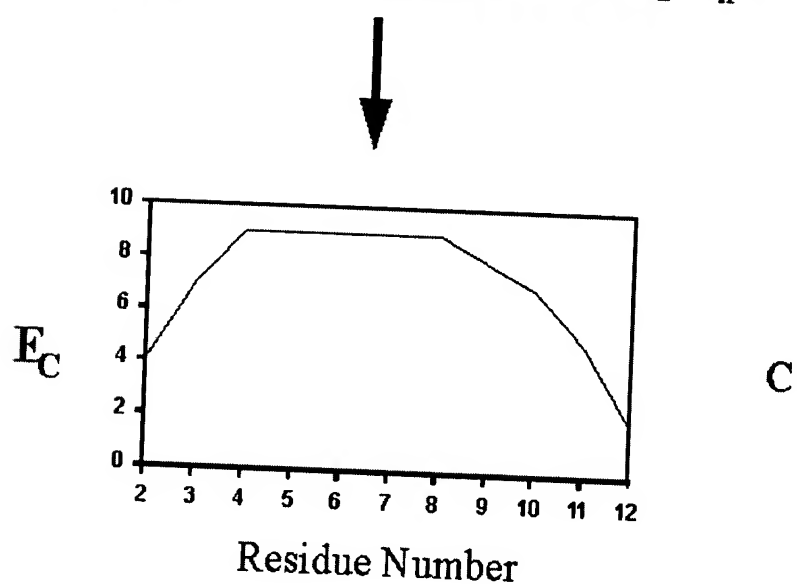
“Protein Z”



A



B



C

FIG. 2

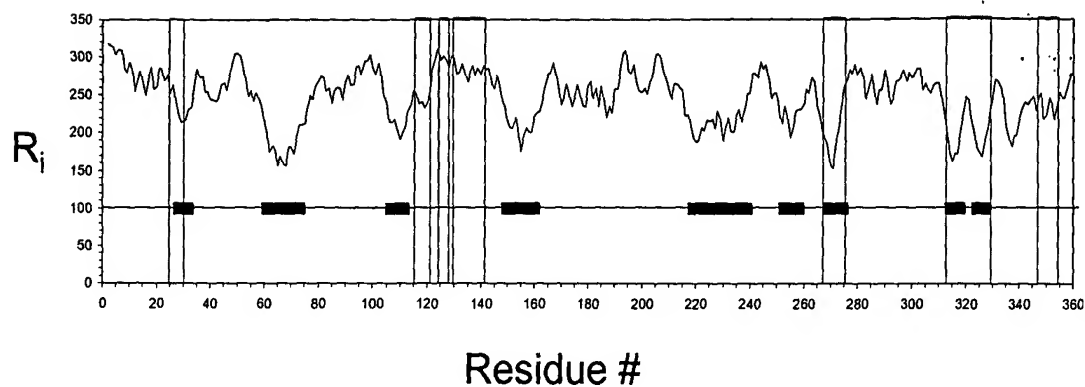
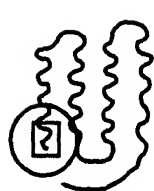
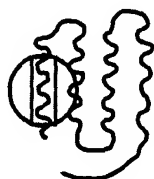


FIG. 22



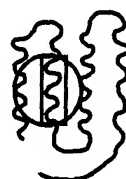
X

Rejected
Fragment size
is less than 15



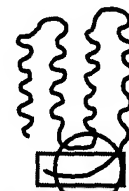
O

Accepted
Fragment is > 15
residues and fits
into the sphere



O

Accepted
Fragment is > 15
residues and fits
into the sphere



X

Rejected
Fragment does not
fit into the sphere

FIG. 23